UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency Office of Pesticide Programs

MEMORANDUM

12/3/2019

SUBJECT: Acute Toxicity Review for Concrobium Mold Control, EPA Reg. No.: 82552-G

FROM: Joseph Williams Jr.
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THRU: Karen P. Hicks, Team Leader
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TO: Jacqueline Hardy, PM Team 34 / Stacey Grigsby
Regulatory Management Branch II
Antimicrobials Division (7510P)

Registrant: Siamons International, Inc.		
Decision No.: 552753	Submission No.: 1036690	E-Sub No.: 40557
DP No.: 454101	Action Code: A540	
MRID No(s).: 50821705,-06,-07,-08-09-10		

Formulation from label			
PC code(s)	CAS #(s)	Active Ingredient(s)	% weight
073506	497-19-8	Sodium Carbonate	1.0%
		Other Ingredients	99.0%
		Total	100%

I. BACKGROUND

The Registrant, Siamons International, Inc., has submitted an application for pesticide registration for their product: Concrobium Mold Control EPA Reg. No. 82552-G. This is an end-use product formulated as disinfection against mildewcidal, fungicidal and bactericidal growth in household and commercial use sites.

II. Findings

1. Acute Oral Toxicity

An acute oral toxicity test was conducted with rats to determine the potential for CMC-Plus to produce toxicity from a single dose via the oral route. Under the conditions of this study, the acute oral LD_{50} of the test substance is greater than 5000 mg/kg of body weight in female rats.

2. Acute Dermal Toxicity

An acute dermal toxicity test was conducted with rats to determine the potential for CMC-Plus to produce toxicity from a single topical application. Under the conditions of this study, the single dose acute dermal LD_{50} of the test substance is greater than 5000 mg/kg of body weight in male and female rats.

3.Acute Inhalation Toxicity

An acute inhalation toxicity test was conducted with rats to determine the potential for CMC-Plus to produce toxicity from a single exposure via the inhalation (nose-only exposure) route. Under the conditions of this study, the single exposure acute inhalation LC_{50} of the test substance is greater than 2.36 mg/L in male and female rats.

4. Primary Eye Irritation

Under the conditions of this study, the test substance was classified as mildly irritating to the eye.

5. Primary Skin Irritation

The Primary Dermal Irritation Index (PDII) calculated for this test substance was 2.9, and the test material was moderately irritating.

6. Dermal Sensitization

Based on the results of this study, the test substance is not considered to be a contact dermal sensitizer in the LLNA. Proper conduct of the LLNA was confirmed via a positive response with 25% Hexyl Cinnamic Aldehyde (HCA), a moderate contact sensitizer.

7.The acute toxicity profile of Concrobium Mold Control, EPA Reg. No. 82552-G is currently:

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	50821705	IV	Acceptable
Acute Dermal Toxicity	50821706	IV	Acceptable
Acute Inhalation Toxicity	50821707	IV	Acceptable
Acute Eye Irritation	50821709	III	Acceptable
Primary Dermal Irritation	50821708	III	Acceptable
Dermal Sensitization	50821710	Not a sensitizer	Acceptable

III. PRODUCT LABELING

1. **Signal Word: CAUTION**
2. **The statement, "Keep Out of Reach of Children (KOROC)", is required. It should appear immediately above the front-panel signal word "Caution".**
3. **In accordance with the Agency's *Label Review Manual* (https://www.epa.gov/sites/production/files/2017-09/documents/lrm-complete-aug-2017.pdf) the First Aid and human-hazard precautionary statements in the submitted label (marked 6/26/19) are acceptable:**

HAZARDS TO HUMANS AND DOMESTIC ANIMALS:

Causes moderate eye irritation. Avoid contact with eyes, skin, or clothing. Wear googles or safety glasses, gloves, and protective clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

4. **FIRST AID:**

IF ON SKIN OR CLOTHING: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

IF IN EYES: Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. Call a poison control center or doctor for treatment advice.

IF INHALED: Move a person to fresh air. If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. Call a poison control center or doctor for treatment advice

IF SWALLOWED: Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to by a poison control center or doctor. Do not give anything to an unconscious person.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OCSPP 870.1100)

Product Manager:

MRID No.: 50821705 **Study Completion Date:** 04/04/2019

Study No.: 49675

Testing Laboratory: Product Safety Labs, Dayton, NJ.

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160): Included

Test Material: CMC-Plus

Dose levels: 5000 mg/kg bw

Animals: Rat, Sprague-Dawley

Number/Sex: 3 Females

Age: 9-10 weeks

Weight: 180-197 grams

Source: SAGE Labs

Method: OCSPP 870.1100; OECD 425

Summary:

1. **Estimated LD_{50}:** >5000 mg/kg bw
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviations from protocol: None.

Results:

Gavage administration of the test material was given as received to three fasted animals as provided in Table 1. An initial limit dose of 5000 mg/kg was administered to one rat by oral gavage. Due to the absence of mortality in this rat, two additional rats received the same dose level. Since these animals survived, no additional animals were tested. Following administration, there were no clinical signs of toxicity, and all animals appeared active and healthy during the 14-day observation period. No gross abnormalities were noted when the animals were necropsied at the conclusion of the study.

Table 1. Reported Mortality – Limit Test

Dosing Sequence	Dose Level (mg/kg bw)	Short-Term Outcome	Long-Term Outcome
1	5000	O	O
2	5000	O	O
3	5000	O	O

O = Survival; X = Death

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OCSPP 870.1200)

Product Manager: **Reviewer:** T.C. Marshall

MRID No.: 50821706 **Study Completion Date:** 04/04/2019

Study No.: 49676

Testing Laboratory: Product Safety Labs, Dayton, NJ.

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160): Included

Test Material: CMC-Plus

Dose levels: 5000 mg/kg bw

Animals: Rat, Sprague-Dawley

Number/Sex: 5 Males and 5 females

Age: 10-11 weeks

Weight: Males: 317-354 grams; Females: 219-227 grams

Source: SAGE Labs

Summary:

1. **Estimated LD_{50}:** >5000 mg/kg bw
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviations from Guideline 870.1200:

None.

Results:

Five thousand milligrams of test substance per kilogram of body weight was applied as received for a 24-hour dermal exposure to previously clipped skin (2 × 3 in. application site for all rats; about 10% of the total body surface area) (Table 1). All animals survived test substance administration, gained body weight, and appeared active and healthy during the study. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period. Under the conditions of this study, the single dose acute dermal LD_{50} of the test substance is >5000 mg/kg by weight in male and female rats.

Table 1. Mortality

Nominal dose (mg/kg bw)	Number Dead / Number Tested		
	Males	Females	Combined
5000	0 / 5	0 / 5	0 / 10

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OCSPP 870.1300)

Product Manager:

MRID No.: 50821707 **Study Completion Date:** 03/25/2019

Study No.: 49677

Testing Laboratory: Product Safety Labs, Dayton, NJ.

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160): Included

Test Material: CMC-Plus

Concentrations: Chamber (gravimetrically determined): 2.36 mg/L

Nominal: 5.00 mg/L.

Chamber Type: Nose-only

Animals: Rat, Sprague-Dawley-derived

Sex: 5 Males and 5 Females

Age: 9-10 weeks at exposure

Weight: Males: 296-314 g; Females: 182-227 g

Source: SAGE® Labs

Method: OCSPP 870.1300; OECD 403

Summary:

1. **LC_{50}:** Males: >2.36 mg/L

   Females: >2.36 mg/L
2. **Mean MMAD:** 2.58 µm (GSD = 2.49)
3. **Toxicity Category:** IV

4. **Classification:** Acceptable

Deviations from Guideline 870.1300: None

Results:

The table below gives the mortality following a four-hour nose-only inhalation exposure to a mean gravimetric concentration of 2.36 mg/L of the aerosolized test substance. All animals survived exposure to the test atmosphere and gained weight during the study. Following exposure, all rats exhibited irregular respiration. However, all animals recovered by Day 1, and appeared active and healthy for the remainder of the 14-day observation period. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the study.

Reported Mortality

Exposure Concentration (mg/L)	Number dead / Number tested		
	Males	Females	Combined
2.36	0 / 5	0 / 5	0 / 10

Chamber Atmosphere

Mean (±SD) Exposure Conc. (mg/L)	Mean MMAD (µm)	Mean GSD	% of Particles < 3.3 µm
2.36 ± 0.41 (Range: 1.80–2.95)	2.58 (2.31, 2.85)	2.49 (2.48, 2.49)	53.8 (59.0, 48.5)

Chamber Environment

Exposure Level (mg/L)	2.36
Chamber Volume (L)	28
Total Airflow Rate (Lpm)	36
Temperature (°C)	19
Relative Humidity (%)	40-46

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OCSPP 870.2500)

Product Manager:

MRID No.: 50821709 **Study Completion Date:** 03/27/2019

Study No.: 49679

Testing Laboratory: Product Safety Labs, Dayton, NJ.

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160): Included

Test Material: CMC-Plus

Dosage: 0.5 mL

Animals: Rabbit, New Zealand albino strain

Sex: 3 Females

Age: 13 weeks

Weight: 2156-2292g

Source: Robinson Services Inc.

Summary:

1. **Toxicity Category:** III
2. **Classification:** Acceptable

Deviations from Guideline 870.2500: None

Results:

The table below provides the individual Draize scores from four-hour dermal exposures of three female rabbits to 0.5 mL of the test material applied as received to intact clipped application sites measuring 6 cm^2. Within 24 hours of patch removal, all three treated sites exhibited very slight to well-defined erythema and very slight edema. The overall incidence and severity of irritation decreased

gradually with time. All animals were free of erythema and edema by Day 10 and desquamation resolved by Day 14. The Primary Dermal Irritation Index (PDII) calculated for this test substance was 2.9, and the test material was moderately irritating.

Individual Dermal Irritation Scores following the four-hour exposure

Animal No.	Sex	Erythema / Edema			
		Time After Patch Removal			
		60 minutes	24 hours	48 hours	72 hours
3501	F	1 / 1	2 / 1	2 / 1	2 / 1
3502	F	2 / 1	2 / 1	2 / 1	2 / 1
3503	F	1 / 1	2 / 1	2 / 1	2 / 2

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (OCSPP 870.2400)

Product Manager:

MRID No.: 50821708 **Study Completion Date:** 03/08/2019

Study No.: 49678

Testing Laboratory: Product Safety Labs, Dayton, NJ.

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160): Included

Test Material: CMC-Plus

Dosage: 0.1 mL

Animals: Rabbit, New Zealand albino strain

Sex: 3 Females

Age: 13-14 weeks

Weight: 2320-2383g

Source: Robinson Services Inc.

Summary:

1. **Toxicity Category**: III
2. **Classification**: Acceptable

Deviations from Guideline 870.2400 and other comments: None noted.

Results:

The tables below provide the results ("positive" irritation and mean total irritation scores) following instillation of 0.1 mL (0.1 mg/kg bw) of the undiluted test material into the right eye of three rabbits. Prior to instillation both the treated and control eyes of each animal were topically anesthetized with 0.5% Tetracaine Hydrochloride Ophthalmic Solution. All animals appeared active and healthy and gained body weight during the study. Apart from the eye irritation noted below, there were no other signs of gross toxicity, adverse clinical effects, or abnormal behavior. Twenty-four hours after test substance instillation, two treated eyes exhibited corneal opacity (Grade = 1), and 'positive' conjunctivitis was observed in one treated eye at one hour. There was no iritis observed in any treated eye during the study. The overall incidence and severity of irritation decreased gradually with time. Positive irritation cleared from both treated eyes by 48 hours. All animals were free of ocular irritation by 72 hours (study termination). The Maximum Mean Total Score was 7.3 at one and 24 hours. Under the conditions of this study, the test substance was classified as mildly irritating to the eye.

Incidence of Irritation

Time Post-Instillation	No. of Animals Testing "Positive" / No. of Animals Tested			
	Corneal Opacity	Iritis	Conjunctiva [a]	
			Redness	Chemosis
1 hour	0 / 3	0 / 3	0 / 3	1 / 3
24 hours	2 / 3	0 / 3	0 / 3	0 / 3
48 hours	0 / 3	0 / 3	0 / 3	0 / 3
72 hours	0 / 3	0 / 3	0 / 3	0 / 3

[a] Redness or chemosis score of 1 not considered a "positive score" according to EPA 870.2400.

Severity of Irritation

Time Post Instillation	Mean Total Score [a]
1 hour	7.3
24 hours	7.3
48 hours	2.0
72 hours	0.0

[a] Draize method of scoring (1944).

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (OCSPP 870.2600)

Product Manager:

MRID No.: 50821710 **Study Completion Date:** 04/19/2019

Study No.: 49680

Testing Laboratory: Product Safety Labs, Dayton, NJ.

Author: Carolyn Lowe, LATG

Quality Assurance (40 CFR §160): Included

Test Material: CMC-Plus

Positive Control Material: alpha-Hexylcinnamaldehyde (HCA; ≥95%), undiluted

Species: CBA/J Mouse

Number/Sex: 23 Females (8 preliminary; 5 test animals, 5 naïve controls, 5 positive controls)

Weight: 17.7-22.4 g (test and naïve control groups)

Age: 9 Weeks

Source: Envigo RMS, Inc.

Method: Local Lymph Node Assay (LLNA); Neat (100% concentration as received) selected based on preliminary irritation/toxicity testing.

Summary:

1. CMC-Plus was not a sensitizer under the conditions of this study.

2. Classification: Acceptable

Deviations from Guideline 870.2600: None

Results:

Stimulation Indices (SI) were calculated using the adjusted group mean DPM value for the test or positive control mice as the numerator and the adjusted group mean DPM value from the vehicle control mice as the denominator; the mean SI ± SD was calculated for each experimental group.

Animal Group	Dose Preparation	Average Net DPM	Number of Mice	SI
Vehicle Control	1% Pluronic® L92	1668	5	—
Positive Control	25% alpha-hexylcinnamaldehyde (≥95%) in 1% Pluronic® L92	12348	5	7.40
100% Test Substance	100% test material	1712	5	1.03

An SI in excess of 3.0 was not observed in the Test Material group, indicating that CMC-Plus was negative for dermal sensitization at 100% concentration (neat).

The Positive Control had an SI of 7.40 which validates the test method.